

## APPENDIX I

EXEMPLARY PORTIONS OF HGS EVIDENCE DEVOTED TO  
EXPERIMENTATION TO TRY TO COMPLETE THE VEGF2 INVENTION

Further experimentation suggested by Dr. Mattick in order to understand the VEGF2 invention or how to make it work:

AJM1 3.15	Computer analysis of sequence for signal peptide.
AJM1 3.16-19	Expression of protein from DNA
AJM1 3.18	Overcoming obstacle of realizing that protein doesn't express because signal sequence is missing or faulty.
AJM1 3.33	Experimentation to express a biologically active VEGF2
AJM1 3.34	Experimentation to obtain VEGF2 polynucleotide sequences.
AJM1 4.3-4.13	Experimentation to express VEGF2 notwithstanding "the fact that the signal sequence information was incomplete" in the opposed application.
AJM1 4.15-4.16	Confirming biological activity, suggestion of collaboration
AJM1 4.64-4.68	Experimentation to produce fragments analogues and derivatives, and identification of such molecules
AJM1 4.77	Expression of incomplete sequence
AJM1 4.82-4.83	Production of antibodies and determination of VEGF2 activity

Further experimentation suggested by Dr. Gamble in order to understand the VEGF2 invention or how to make it work:

AJG1 5.14-5.19	Assaying for angiogenic properties
AJG1 7.9-7.10	Testing for <i>in vivo</i> or <i>in vitro</i> activity
AJG1 7.11	Distinguishing between growth factors
AJG1 7.20	Antibody production
AJG1 7.35	Experimentation to produce fragments analogues and derivatives

Further experimentation suggested by Dr. Hayward in order to understand the VEGF2 invention or how to make it work:

- ANH1 3.11-3.12      Designing suitable hybridization conditions
- ANH1 3.19-3.21,4.20 Use of heterologous signal sequence
- ANH1 3.25            5' end cloning
- ANH1 3.27            Testing for a biological activity
- ANH1 3.29            Testing VEGF2 in proliferation, angiogenesis and wound healing assays
- ANH1 3.34            Testing of receptor binding
- ANH1 4.4             Activity assays
- ANH1 4.26-4.27      Redesigning Example 2 in the application in order to attempt to achieve the results that were reported

Further experimentation suggested by Dr. Rapoport in order to understand the VEGF2 invention or how to make it work: (essentially entire declaration, devoted to identifying signal peptide defect in patent application, and then trying to overcome it.)

Further experimentation suggested by Dr. Aaronson in order to understand the VEGF2 invention or how to make it work:

- ASA1 at 16            Engineering a heterologous signal sequence

Further experimentation suggested by Dr. Power in order to understand the VEGF2 invention or how to make it work: (Entire Declaration devoted to signal peptide experiments which are not based on the applications teachings.)

**APPENDIX II**  
**EXEMPLARY PORTIONS OF HGS EVIDENCE DEVOTED TO**  
**CATALOGUING PREDICTIONS IN THE PATENT APPLICATION**

Cataloging by Dr. Mattick of statements, unsupported predictions, and other unsupported excerpts of the HGS application:

- AJM1 3.25, 3.30-3.31 (Alleged uses of VEGF2 - no supporting data)
- AJM1 3.32 and JSM-4 Table 1 (essentially a table of contents for application.)
- AJM1 4.3 and 4.5-4.11 (overcoming signal sequence issue)
- AJM1 4.18-4.24 (biological properties of VEGF2 and theoretical uses)
- AJM1 4.30 and 4.39 (hybridization conditions and control thereof)
- AJM1 4.67 (testing for activity)
- AJM1 4.70 and 4.73 (gene therapy and treatments)
- AJM1 4.77 (heterologous signal sequence usage)
- AJM1 4.82-4.83 (antibody production)
- AJM1 4.108 (antagonists)

Cataloging by Dr. Gamble of predictions and other unsupported excerpts of the HGS application:

- AJG1 6.5 (prediction of processing)
- AJG1 6.6 (expression systems)
- AJG1 6.7 (activity assays)
- AJG1 6.8 - 6.8.11 (list like Mattick)
- AJG1 7.11 (assays for fragments, etc)
- AJG1 7.15-7.18 (angiogenic assays)
- AJG1 7.20 (generation of antibodies)
- AJG1 7.24 (prediction of processing)
- AJG1 7.35 (generation of fragments)

Cataloging by Dr. Hayward of predictions and other unsupported excerpts of the HGS application:

- ANH1 3.6 (activities fo VEGF2 and/or fragments, etc.)
- ANH1 3.11 (hybridization conditions)
- ANH1 3.15 (expectation of secretion)

ANH1 3.19-3.21 (use of heterologous signal sequence)

ANH1 3.22 (processing)

ANH1 3.27-3.30 (activities and uses of VEGF2)

ANH1 3.34 & 3.35 (binding of receptors)

ANH1 3.37 (uses of fragments and antibodies)

ANH1 4.4 (assays and activities)

Cataloging by Dr. Rapoport of predictions and other unsupported excerpts of the HGS application:

ATR1 at 11 (prediction of processing)

ATR1 at 12 (heterologous signal sequence)

ATR1 at 18 (prediction of a secreted growth factor)

Cataloging by Dr. Aaronson of predictions and other unsupported excerpts of the HGS application:

ASA1 at 5 (prediction of secretion)

ASA1 at 6 (proteolytic processing)

ASA1 at 16 (heterologous signal sequence)

AUSTRALIA

*Patents Act 1990*

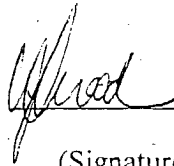
IN THE MATTER OF Australian Patent  
Application Serial No. 696764 by Human  
Genome Sciences, Inc.

-and-

IN THE MATTER OF Opposition thereto by  
Ludwig Institute for Cancer Research

THIS IS Exhibit FJB-1  
referred to in the Statutory Declaration  
of Francis John Ballard  
made before me

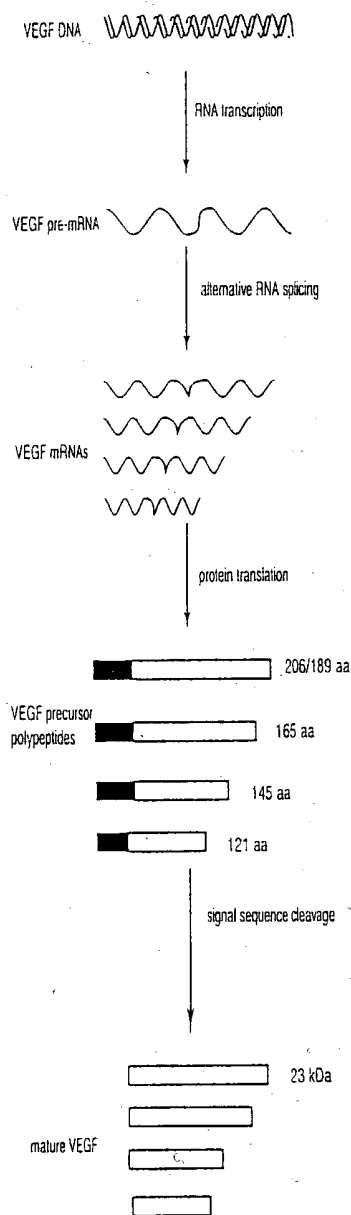
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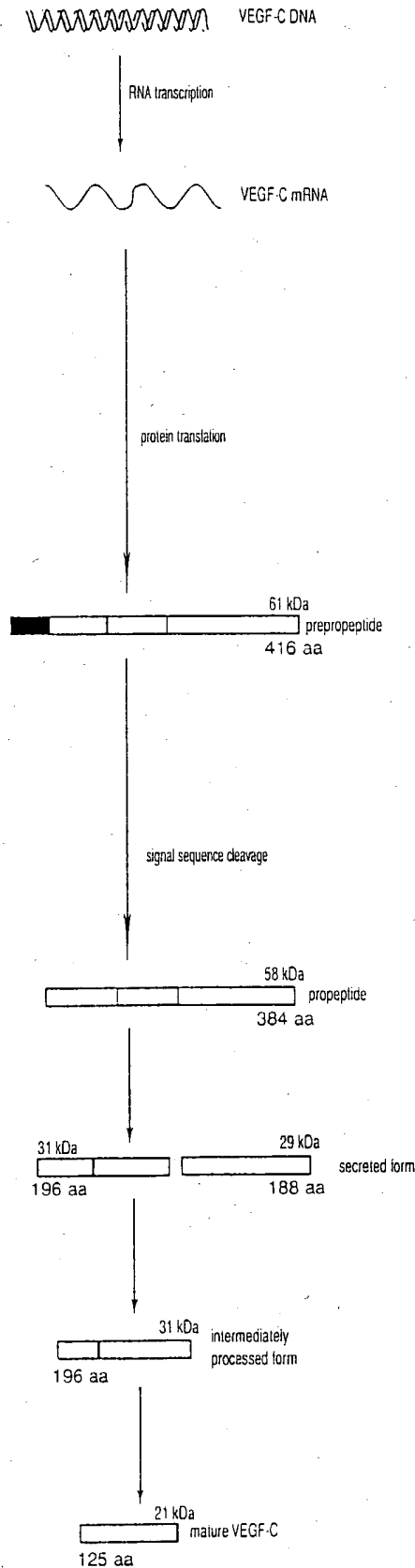
(Signature of Witness)

Lynette C. Kinkwood (Pharmacist)

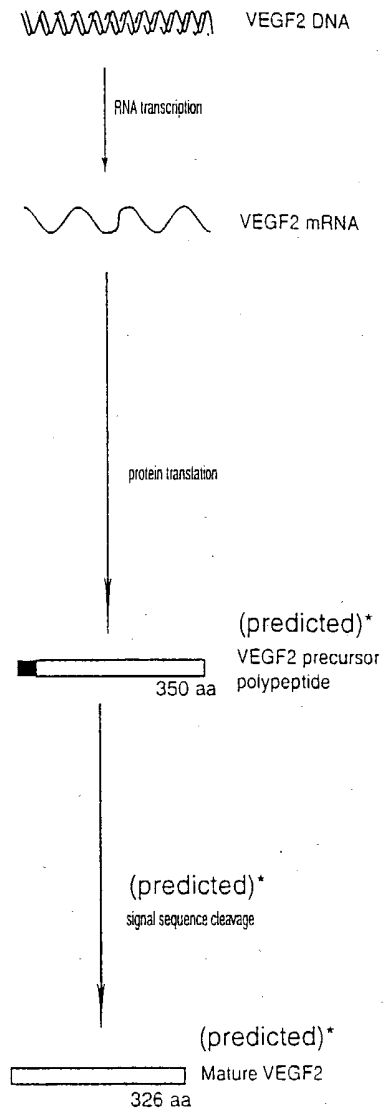
### A Prior Art VEGF



### B Alitalo VEGF-C



### C HGS VEGF2 (opposed application)



\*No evidence in opposed application. Alitalo declarations show that this does not happen.